

U.S.S.N. 09/821,203  
Filed: March 29, 2001  
AMENDMENT AND RESPONSE TO OFFICE ACTION

### In the Claims

1-20 (previously canceled)

21. (presently amended) A ~~An improved~~ method of detecting changes in the expression of genes associated with a particular state, disease or disorder in a microarray, wherein the genes comprise an E-box regulatory sequence, or encode proteins or cofactors that bind to the E-box regulatory sequence, the improvement comprising

a) providing an array of genes comprising an E-box regulatory sequence in its promoter or interacting with a gene binding to the E-box regulatory sequence a set of primers for reacting with a nucleic acid sequence in the genes in the microarray, with the sequences having a length of between 480 and 700 base pairs and a melting point of between 75 and 85°C; and comprising a non-consensus sequence so that there is no detectable hybridization with homologous sequences;

b) providing a reacting the set of primers for use in detecting changes in expression of genes comprising an E-box regulatory sequence in its promoter or interacting with a gene binding to the E-box regulatory sequence having a length between 480 and 700 base pairs length and a melting point between 75 and 85°C, wherein the primers include non-consensus sequence with protein coding sequence so that there is no detectable hybridization between homologous genes comprising a label with the genes to amplify the nucleic acid sequence to form amplicons;

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c) ~~providing the array of genes comprising an E-box regulatory sequence in its promoter or interacting with a gene binding to the E-box regulatory sequence and sequences encoding proteins associated with a particular state, disease or disorder further comprising housekeeping genes whose expression does not change significantly as the state, disease or disorder changes~~ arraying the amplicons produced from the reaction in step (b) onto a solid support; and

d) ~~reacting the primers amplicons with the genes~~ a labeled probe comprising all or a portion of the non-consensus sequence; and

e) detecting levels of hybridization between the amplicons and the labeled probe, thereby detecting levels of gene expression.

22. (presently amended) ~~A~~ The method of claim 21 for screening for differential expression of one or more E-box regulatory genes or genes interacting with genes binding to the E-box regulatory sequence, comprising:

a) providing a first library of genes associated with a particular disease, disorder or state,

b) providing a second library of DNA of genes obtained from cells having a different state or expressed to a compound to be tested,

c) detecting or measuring expression of selected genes in the first and second library using the method of claim 21,

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- d) comparing the expression of the selected genes in the first and second libraries, and
  - e) detecting which genes have altered expression in the second DNA library.
23. (presently amended) The method of claim 22 wherein the state is selected from the group consisting of age, cancer and diseases or disorders of the cardiovascular, neurological, and musculoskeletal systems.
24. (original) The method of claim 22 wherein the compound is a drug or toxin.
25. (original) The method of claim 22 further comprising normalizing results of expression by comparison with levels of expression of housekeeping genes.
26. (presently amended) A The method of claim 21 for determining the effect of a compound, disease or state of an individual comprising:
- a) providing a DNA library including one or more E-box regulatory genes or genes that interacting with genes binding to the E-box regulatory sequence, wherein the genes are obtained from the individual after treatment of the individual, cells or tissues derived therefrom with the compound or a particular dosage regime of the compound,
  - b) screening the library for changes in levels of expression of the selected genes using the method of claim 21, and
  - c) correlating the changes in expression with the state, disease or disorder prior to treatment.

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27. (original) The method of claim 26 wherein the cells or tissues are treated with one or more compounds *in vitro* prior to making the DNA library.

28. (original) The method of claim 26 wherein the compound is selected from the group consisting of proteins or peptides, sugars or polysaccharides, nucleic acid molecules, and synthetic molecules.

29. (original) The method of claim 26 wherein the library is derived from cells obtained from an individual of a particular age, having a particular disease or disorder, or derived from the neurological system, the cardiovascular system, the musculoskeletal system, or cancerous tissues.